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Title of the Invention: External Medicine for Skin

Claims:

1. An external medicin for skin, comprising the following components (a) and (b):

(a) a perilla oil; and

(b) one or more selected from dipotassium glycyrrhizinate, stearyl glycyrrhetinate, phospholipid, hydrogenated phospholipid, cholesterol, perilla extract, Houttuynia cordata extract, saxifragacede extract, maltitol, sorbitol, and mannitol.

[Detailed Description of the Invention]

[0001]

[Industrial Application Field]

The present invention relates to an external medicine for skin and more particularly to an external medicin for skin capable of preventing inflammation and drying of the skin and exhibiting an excellent effect against a dry skin and skins of similar symptoms.

[0002]

[Prior Art]

As efficacious components so far used for preventing the inflammation and drying of the skin there are known allantoin, aloe extract, placenta extract, carrot extract, hyaluronic acid, collagen, and amide acids. However, with external medicines for skin containing these efficacious components, it is impossible to obtain a satisfactory effect and the development of an external medicine for skin which exhibits a superior action has been desired.

[0003]

On the other hand, perilla oil has a high content of α-linolenic acid which is a kind of ω-type highly unsaturated fatty acid. It is known that when applied to the skin, perilla oil moistens the skin to prevent drying of the skin. The α-linolenic acid is metabolized in the body to eicosapentaenoic acid or docosahexaenoic acid. At present it is known that these ω-3 type highly unsaturated fatty acids are effective in decreasing the production of leukotriene which exhibits an anti-cancer effect and induces an allergic reaction. Thus, they are now gaining attention.

[0004]

[Problems to be Solved by the Invention]

Taking note of the above actions of perilla oil, the

present inventors tried to mix it into an external medicine for the skin, especially an external medicine for the skin capable of remedying inflammation and drying of the skin. However, the skin inflammation and dryness remedying effect obtained in case of using perilla oil alone cannot be said satisfactory. Besides, due to the influence of other bases, etc., the effect inherent in perilla oil cannot be exhibited to a satisfactory extent. This has been the actual situation.

[0005]

If perilla oil is used at a high concentration for the purpose of attaining a more outstanding effect, a limit is encountered in point of function and effect. Conversely, due to the development of color and smell peculiar to perilla oil, a limit is encountered also in point of its content and dosage form as product.

[0006]

[Means for Solving the Problems]

In view of the above-mentioned circumstances and for deriving the effects of perilla oil to a satisfactory extent, the present inventors have made earnest studies. As a result, we found out that an excellent skin inflammation and dryness remedying effect was exhibited stably and synergistically by combining perilla oil with a

specific compound. In this way we completed the present invention.

[0007]

More specifically, the present invention provides an external medicine for skin comprising the following components (a) and (b):

(a) a perilla oil; and

(b) one or more selected from dipotassium glycyrrhizinate, stearyl glycyrrhetinate, phospholipid, hydrogenated phospholipid, cholesterol, perilla extract, Huttuynia cordata extract, saxifragacede extract, maltitol, sorbitol, and mannitol.

[0008]

The perilla oil as an essential component (a) in the present invention results from extraction from seeds of Perilla frutescens Britton var. japonica Hara and other plants of the same family (Perilla family) by a conventional method. The method is not specially limited. Perilla oil having a concentrated and increased content of α-linolenic acid as a main component, or an oil composition comprising a mixture thereof with other components, is also included.

[0009]

Perilla oil may be mixed as it is into the external

medicine for skin according to the present invention or may be used after purification by steam distillation, treatment with activated carbon, or treatment with acid clay.

[0010]

The content of perilla oil in the cosmetic of the present invention is 0.0001-10 wt% (hereinafter referred to merely as "%"), preferably 0.01-5%. If its content is lower than 0.0001%, a satisfactory effect may not be obtained, and even if perilla oil is used in an amount exceeding 10%, there will not be attained any further enhancement of effect, but rather there may occur problems concerned with product such as coloration, development of smell, and precipitation in a certain dosage form.

[0011]

On the other hand, the other essential component (b) used in the present invention is one or more selected from glycyrrhizinic acid, glycyrrhetinic acid, phospholipid, hydrogenated phospholipid, cholesterol and its derivative and salts thereof, perilla extract, Houttuynia cordata extract, saxifragacede extract, maltitol, sorbitol, and mannitol.

[0012]

The component (b) has heretofore been incorporated in external medicines for skin and no limitation is placed on

their sources and how to acquire them. Commercially available ones are employable.

[0013]

The content of the above specific components in the external medicine for skin according to the present invention (as dry solids in the case of an extract) is 0.00001-10%, more preferably 0.001-3%. If the content of the specific components is lower than 0.00001%, a satisfactory effect may not be obtained, while even if the specific components are used in an amount exceeding 10%, there will not be attained any further enhancement of effect, but rather a bad influence may occur in point of pharmaceutical preparation.

[0014]

Further, in the external medicine for skin of the present invention there may be further incorporated, in addition to the above essential components and as necessary within the range not spoiling the effect of the invention, components used in conventional external medicines for skin such as aqueous component, powder, surfactant, oil, humectant, alcohols, pH controller, preservative, pigment, antioxidant, infrared absorber, thickener, fragrance, and cosmetic component.

[0015]

The external medicine for skin of the present invention can be produced by mixing the components (a) and (b) and in accordance with a conventional method. It can be provided in the form of not only such cosmetics as milky lotion, cream, skin lotion, cosmetic solution, cleansing, pack, detergent, and foundation, but also medicines or quasi-medicines, including dispersion, ointment, cream, and liquid preparation for external use.

[0016]

[Examples]

The present invention will be further described below by way of working Examples, but the invention is not limited to the following Examples.

[0017]

Example 1: Milky Lotion

Milky lotions were produced in accordance with the following formulation and method and were then evaluated by a carragen plantar edema inibition test.

[0018] (Formulation)

Table 1

ingredient (wt%)	present invention				comparative				
	1	2	3	4	1	2	3	4	5
(1) squalene	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
(2) vaseline	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
(3) beeswax	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
(4) sorbitane sesquioleate	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
(5) polyoxyethylene oleyl ether (20E.O.)	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
(6) 1, 3-butylene glycol	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
(7) perilla oil *1	1.0	1.0	1.0	1.0	1.0	---	---	---	---
(8) dipotassium glycyrrhizinate*2	0.2	---	---	---	---	0.2	---	---	---
(9) perilla extract*3	---	0.2	---	---	---	---	0.2	---	---
(10) Houttuynia cordata extract*4	---	---	1.0	---	---	---	---	1.0	---
(11) saxifragacede extract *5	---	---	---	1.0	---	---	---	---	1.0
(12) ethylalcohol	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
(13) preservative	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
(14) fragrance	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
(15) xanthan gum (2%aq.)	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0
(16) purified water	bl	bl	bl	bl	bl	bl	bl	bl	bl

bl: balance

(*1) oil obtained from perilla seeds

(*2) a product of Maruzen Seiyaku Co.

(*3) obtained by adding 100 parts of 50V/V% ethanol to 10 parts of Perilla leaves, conducting extraction for 3 days under occasional agitation at room temperature, and freeze-drying the resulting extract

(*4) obtained by adding 100 parts of 50 V/V% 1,3-butylene glycol to 10 parts of a terrestrial portion of Houttuynia cordata

and conducting extraction for 7 days at room temperature

(*5) obtained by adding 100 parts of 1,3-butylene glycol to 10 parts of saxifragfacede leaves and conducting extraction for 3 days under occasional agitation at room temperature.

[0019] (Method for Production)

A. The ingredients (6), (8)-(12) and (16) are mixed under heating and are held at 70°C.

B. The ingredients (1)-(5), (7), (13) and (14) are mixed under heating and are held at 70°C.

C. The mixture obtained in B is added to A, followed by mixing, then the ingredient (15) is added and emulsification is allowed to take place uniformly, followed by cooling to 30°C to afford a milky lotion.

[0020] (Evaluation)

Carragheenin Plantar Edema Inhibition Test

A 1% carragheenin isotonic sodium chloride solution as an inflammation inducing agent is injected subcutaneously into rear leg plantar portions of a group of ten Wistar male rats of 6-7 weeks old, allowing edema to be formed. 0.1 ml of the sample is applied to the rats after 2 hours and also just after the injection of carragheenin,

then the plantar volume is measured in 4 hours after the injection of carragheenin to determine a percent edema inhibition relative to a control group.

[0021]

The results o the carragheenin plantar edema inhibition test are shown in Table 2.

[0022]

Table 2

Test Results		Percent Carragheenin Edema Suppression (%)
Present Invention	1	45.8
	2	37.0
	3	39.7
	4	33.6
Com-parative	1	10.2
	2	21.5
	3	8.3
	4	5.0
	5	5.1

[0023]

As is apparent from the results of Table 2, the products 1-4 of the present invention each obtained by mixing perilla oil with any of dipotassium glycyrrhizinate,

perilla extract, sxifragacede extract, exhibit an outstanding edema inhibiting action and have an excellent anti-inflammation effect, in comparison with comparative products 1-5 each obtained by using any of the above ingredients alone.

[0024]

Example 2: Milky Lotion

Milky lotions were produced in accordance with the following formulation and method and were then evaluated by a rough skin remedying test.

[0025] (Formulation)

Table 3

ingredient (wt%)	present invention		comparative			
	5	6	6	7	8	9
(1) squalene	5.0	5.0	5.0	5.0	5.0	5.0
(2) vaseline	2.0	2.0	2.0	2.0	2.0	2.0
(3) beeswax	0.5	0.5	0.5	0.5	0.5	0.5
(4) sorbitane sesquioleate	0.8	0.8	0.8	0.8	0.8	0.8
(5) polyoxyethylene oleyl ether (20E.O.)	1.2	1.2	1.2	1.2	1.2	1.2
(6) 1, 3-butylene glycol	5.0	5.0	5.0	5.0	5.0	5.0
(7) perilla oil *1	0.2	0.2	0.2	---	---	---
(8) maltitol *2	0.1	---	---	0.1	---	---
(9) hydrogenated soybean*3 phospholipid	---	0.5	---	---	0.5	---
(10) ethylalcohol	5.0	5.0	5.0	5.0	5.0	5.0
(11) preservative	0.2	0.2	0.2	0.2	0.2	0.2
(12) fragrance	0.1	0.1	0.1	0.1	0.1	0.1
(13) xanthan gum (2%aq.)	20.0	20.0	20.0	20.0	20.0	20.0
(14) purified water	bl	bl	bl	bl	bl	bl

(*1) oil obtained from perilla seeds

(*2) a product of Rinpara Shoji Co.

(*3) a product of Nikko Chemicals Co.

[0026] (Method for Production)

A. The ingredients (6), (8)-(10) and (14) are mixed under heating and are held at 70°C.

B. The ingredients (1)-(5), (7) and (12) are mixed under heating and are held at 70°C.

C. The product obtained in B is mixed with A, then the ingredient (13) is added, allowing emulsification to take place uniformly, followed by cooling to 30°C to afford a milky lotion.

[0027] (Evaluation)

Rough Skin Remedying Test

For ten healthy persons of 24 to 40 years old as panel members, the state of the skin before inducing an experimental rough skin was photographed using a microscope camera and the score thereof was determined in accordance with the following criterion. The experimental rough skin was induced by treating the upper arm flexor side with a mixture (1:1) of ether and acetone. Thereafter, the test lotions were applied twice a day, morning and night, over a period of seven days, and the score of the state of skin was determined in the same way as above in 3, 5, and 7 days

after the occurrence of rough skin.

[0028] (Criterion)

Score

1 Skin grooves are not clear and the exfoliation of keratin is conspicuous.

2 Skin grooves are somewhat not clear and the exfoliation of keratin is recognized.

3 Skin grooves are recognized, but are shallow or strongly unidirectional.

4 Skin grooves are recognized and are somewhat mesh-like.

5 Mesh-like regulated grooves are recognized.

[0029]

The results of the rough skin remedying test are shown in Table 4.

[0030]

Table 4

Test Results		Rough Skin Remedying Score			
		before roughen-ing	after 3 days	after 5 days	after 7 days
Present Invention	5	3.4	1.5	2.6	3.9
	6	3.0	1.3	2.4	4.0
Com-parative	6	3.3	1.3	2.3	2.9
	7	3.4	1.3	2.0	2.5
	8	3.3	1.3	2.3	2.9
	9	3.4	1.3	1.9	2.2

[0031]

As is apparent from the results of Table 4, the products 5 and 6 of the present invention each obtained by mixing perilla oil with maltitol or hydrogenated soybean phospholipid exhibit an outstanding rough skin remedying action and have an excellent effect in comparison with the comparative products 6-8 each containing any of the said ingredients alone and the comparative product 9 not containing any of them.

[0032]

Example 3: Milky Lotion

Milky lotions were produced in accordance with the following formulation and method and were then evaluated for skin beautifying effect.

[0033] (Formulation)

Invention Product 1 (as described in Example 1)

Invention Product 6 (as described in Example 2)

Comparative Product 1 (as described in Example 1)

Comparative Product 2 (as described in Example 1)

Comparative Product 3 (as described in Example 1)

[0034] (Method for Production)

How to produce these products is as described in Example 1 or Example 2.

[0035] (Evaluation)

Skin Beautifying Effect Test

Fifteen women of 25 to 56 years old as panel members whose face skins were recognized to be dry skins were instructed to apply proper amounts of the test lotions to their faces after face washing twice a day, morning and night, over a period of eight weeks. Then, the resulting effects were evaluated in accordance with the following criterion.

[0036] (Criterion)

Evaluation:

Outstanding Effect ... The dry of the skin was remedied remarkably and there appeared moisture and luster.

Effective ... The dry of the skin was remedied and moisture of the skin was felt.

Somewhat Effective ... The dry of the skin became less conspicuous.

Ineffective ... No change from the state before use.

[0037]

The results of the skin beautifying effect test are shown in Table 5.

[0038]

Table 5

Test Results		Evaluation			
		Outstanding Effect	Effective	Somewhat Effective	In-effective
Present Invention	1	4	11	0	0
	6	5	9	1	0
Com-parative	1	0	5	8	2
	2	0	2	6	7
	3	0	2	8	5

[0039]

As is apparent from the results of Table 5 it is seen that the products 1 and 2 of the present invention each obtained by combining perilla oil with dipotassium glycyrrhizinate or hydrogenated soybean phospholipid exhibit an outstanding dry skin remedying effect and have an outstanding effect.

[0040] Example 4: Skin Lotion

Skin lotions were produced in accordance with the following formulation and method and were found to exhibit an excellent remedying effect against inflammation and drying of the skin.

[0041]

(Formulation)	(wt%)
(1) glycerin	5.0
(2) 1,3-butylene glycol	6.5
(3) polyoxyethylene sorbitan monolaurate (20E.O.)	1.2
(4) ethyl alcohol	8.0
(5) perilla oil	0.01
(6) Perilla extract (Note)	3.0
(7) preservative	0.2
(8) fragrance	0.1
(9) purified water	balance

(Note) a product of Nikko Chemicals Co.

[0042] (Method for Production)

A. The ingredients (3)-(5), (7) and (8) are mixed and dissolved.

B. The ingredients (1), (2), (6) and (9) are mixed and dissolved.

C. The solutions A and B are mixed homogeneously to afford skin lotions.

[0043] Example 5: Pack

A pack was produced in accordance with the following formulation and method. The pack of the present invention

proved to exhibit an outstanding remedying effect against inflammation and drying of the skin.

[0044]

(Formulation)	(wt%)
(1) polyvinyl alcohol	20.0
(2) glycerin	5.0
(3) kaolin	6.0
(4) sorbitol (Note)	0.01
(5) ethyl alcohol	20.0
(6) perilla oil	0.05
(7) preservative	0.2
(8) fragrance	0.1
(9) purified water	balance

(Note) a product of Wako Junyaku Co.

[0045] (Method for Production)

A. The ingredients (1)-(4) and (9) are mixed, heated to 70°C, and agitated.

B. The ingredients (5)-(8) are mixed together.

C. The mixture B is added to and mixed with the mixture A, followed by cooling, to afford a pack.

[0046] Example 6: Detergent

A detergent was produced in accordance with the following formulation and method and was found to have an excellent remedying effect against inflammation and drying

of the skin.

[0047]

(Formulation)	(wt%)
(1) stearic acid	10.0
(2) palmitic acid	8.0
(3) myristic acid	12.0
(4) lauric acid	4.0
(5) oleyl alcohol	1.5
(6) purified lanolin	1.0
(7) fragrance	0.1
(8) preservative	0.2
(9) glycerin	18.0
(10) potassium hydroxide	6.0
(11) perilla oil	0.5
(12) stearyl glycyrrhetinate (Note)	0.05
(13) purified water	balance

(Note) a product of Maruzen Seiyaku Co.

[0048] (Method for Production)

A. The ingredients (9), (10) and (13) are mixed and heated to 70°C.

B. The ingredients (1)-(6), (8), (11) and (12) are mixed and heated to 70°C.

C. The mixture B is added to the mixture A, the temperature is held at 70°C for a while, then after

completion of a saponification reaction, cooling is performed to 50°C, then the ingredient (7) is added, followed by cooling to afford a detergent.

[0049]

[Effect of the Invention]

The external medicine for skin according to the present invention can prevent inflammation and drying of the skin and exhibits an excellent remedying effect against what is called dry skin which shows a dry symptom or a symptom similar thereto.